HEARTS AND KIDNEYS AND SUGARS, OH MY!

A DIABETES UPDATE

Dawn Battise, PharmD, BCACP
Associate Professor
Wingate University School of Pharmacy

OBJECTIVES

Identify new drug approvals related to diabetes management

Compare and contrast non-glucose lowering benefits of antihyperglycemic medications

Recall key updates to the 2023 American Diabetes Association Standards of Care

Apply updated diabetes information to patient scenarios

ABBREVIATIONS

ACR: albumin:creatinine ratio

ACC: American College of Cardiology

ADA: American Diabetes Association

AGA: American Gastroenterological Association

AHA: American Heart Association

ASCVD: atherosclerotic cardiovascular disease

BMI: body mass index

CVOT: cardiovascular outcome trial

CKD: chronic kidney disease

CVD: cardiovascular disease

DPP4i: dipeptidyl-peptidase 4 inhibitor

eGFR: estimated glomerular filtration rate

ESKD: end stage kidney disease

GIP: glucose-dependent insulinotropic polypeptide

GLP1a: glucagon-like peptide 1 agonist

HF: heart failure:

HFpEF: heart failure with preserved ejection fraction

HFrEF: heart failure with reduced ejection fraction

HFSA: Heart Failure Society of America

KDIGO: Kidney Disease Improving Global Outcomes

MACE: major adverse cardiovascular event

MI: myocardial infarction

PVD: peripheral vascular disease

SGLT2i: sodium glucose co-transporter 2 inhibitor

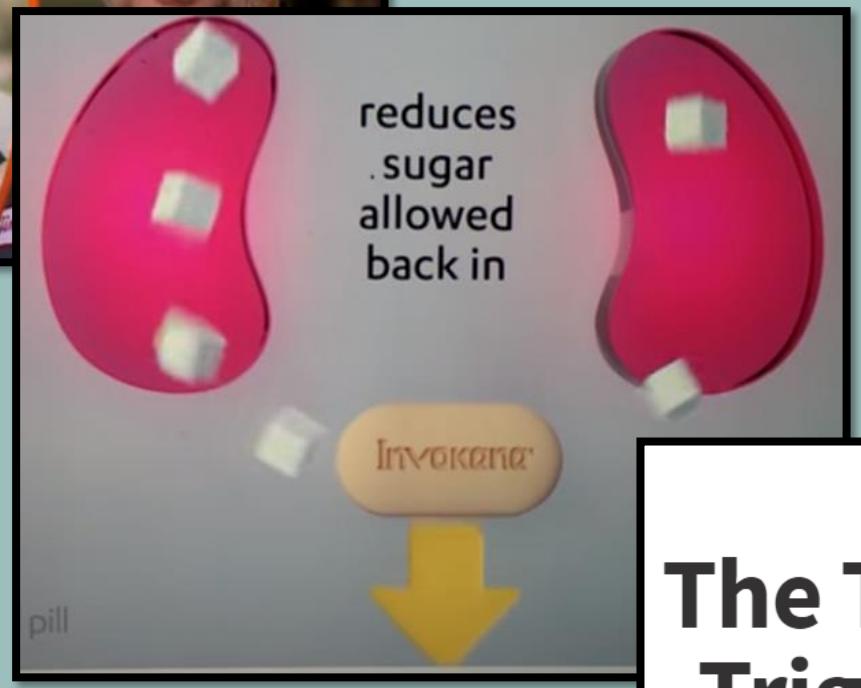
SU: sulfonylurea

T1DM: type 1 diabetes mellitus

T2DM: type 2 diabetes mellitus

TZD: thiazolidinedione

KNOW YOUR WHY



WEBMD HEALTH NEWS

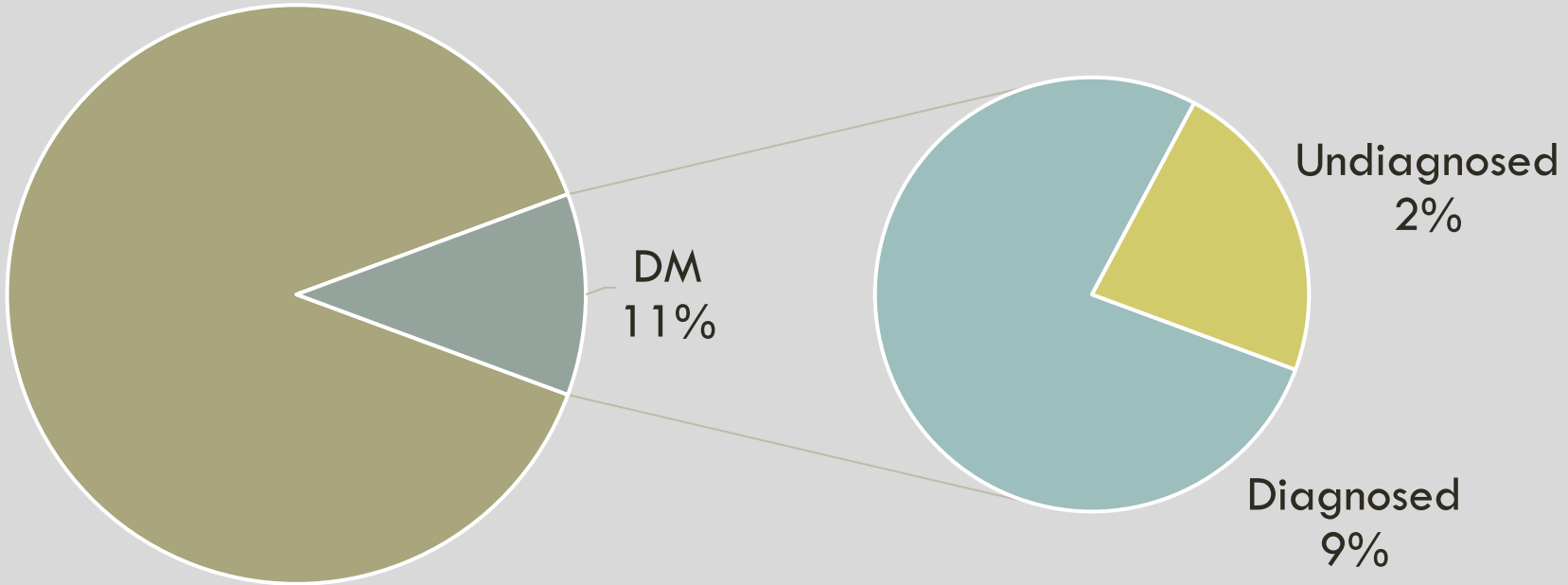
The TikTok Trend That Triggered a Diabetes Drug Shortage

Written by Debbie Koenig

Ozempic TM. Ozempic commercial TM [video]. YouTube. https://www.youtube.com/watch?v=bzlBj90D3YA Published October 13, 2019. Accessed April 21, 2023.
R Trelford. Invokana commercial 2016 [video]. YouTube. https://www.youtube.com/watch?v=R_gp8I-ZyZQ&t=40s Published January 22, 2016. Accessed April 21, 2023.
Keonig D. The TikTok Trend That Triggered a Diabetes Drug Shortage. November 29, 2022. Accessed April 21, 2023.
https://www.webmd.com/obesity/news/20221129/the-tiktok-trend-that-triggered-a-dia1betes-drug-shortage

IMPACT OF DIABETES

% of US population with diabetes



11.3% = 38.3 M

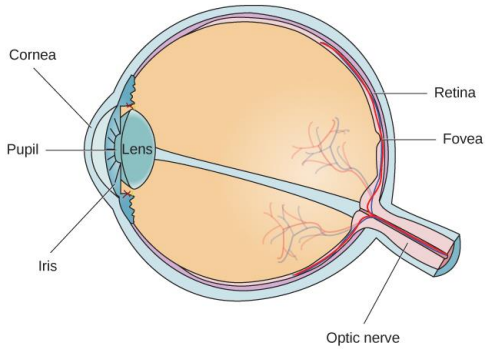
8.7% = 28.7 M

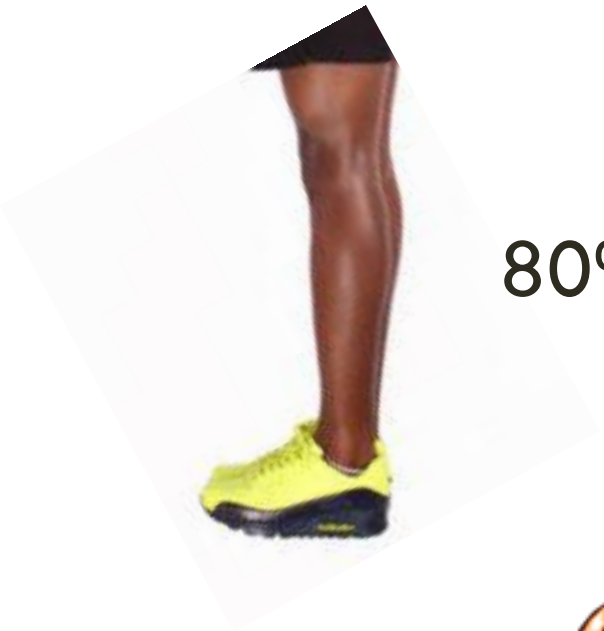
2.3% = 8.5 M

National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States. Centers for Disease Control and Prevention. National Diabetes Statistics Report website. Updated June 29, 2022. Accessed April 21, 2023. https://www.cdc.gov/diabetes/data/statistics-report/index.html.

COMPLICATIONS

#1





80%

2x

#1

National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States – Coexisting Conditions and Complications. Centers for Disease Control and Prevention. National Diabetes Statistics Report website. Updated September 8, 2022. Accessed April 21, 2023. https://www.cdc.gov/diabetes/data/statistics-report/coexisting-conditions-complications.html.
Heart Disease and Stroke. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion website. Updated September 30, 2022. Accessed May 5, 2023. https://www.cdc.gov/chronicdisease/resources/publications/factsheets/heart-disease-stroke.htm#diabetes
Preventing Diabetes Related Amputations. Centers for Disease Control and Prevention. Living with Diabetes website. Updated April 7, 2023. Accessed May 5, 2023..
https://www.cdc.gov/diabetes/library/features/amputations.html#:~:text=Lower%2Dlimb%20amputations%20(LLA),hospitalizations%20due%20to%20amputation%20doubled.

NEW APPROVALS

TEPLIZUMAB

Tzield™ (teplizumab-mzwv)

Indication: delay the onset of Stage 3 T1DM in adults and pediatric patients ≥8 years old with Stage 2 T1DM

Class: CD3-directed antibody

MOA: binds CD3 present on T lymphocytes; may deactivate beta cell autoreactive T lymphocytes among other actions

Dose: based on body surface area; 30 minute IV infusion daily over 14 consecutive days

CI: none

Warnings: cytokine release syndrome, lymphopenia, serious infections

AE: (>10%) lymphopenia, leukopenia, rash, headache

https://tzieldhcp.com/

Tzield [package insert]. Red Bank, NK. Prevention Bio, Inc. 2022.

FINERENONE

Indication: reduce risk of sustained eGFR decline, end stage kidney disease (ESKD), CV death, non-fatal MI, HF hospitalization in adults with chronic kidney disease (CKD) associated with T2DM

Class: non-steroidal mineralocorticoid receptor antagonist (MRA)

MOA: block MR mediated sodium reabsorption and MR overactivation in both epithelial and nonepithelial tissues

Dose: 10 or 20 mg once daily

CI: concomitant CYP3A4 inhibitors; adrenal insufficiency

Warnings: hyperkalemia

AE: (>1%) hyperkalemia, hypernatremia, hypotension

https://www.kerendiahcp.com/

Kerendia [package insert]. Whippany, NJ. Bayer HealthCare Pharmaceuticals, Inc. 2021.

SEMAGLUTIDE

OZEMPIC®
semaglutide injection 0.5mg, 1mg, 2mg

Indication: improve glycemic control in adults with T2DM; reduce the risk of major adverse cardiovascular events (MACE) in adults with T2DM and established CVD

Class: glucagon-like peptide-1 agonist (GLP1a)

MOA: binds to GLP1 receptors stimulates insulin secretion and lowers glucagon secretion, in a glucose-dependent fashion; delays gastric emptying

Dose: 0.25 mg subcut once weekly; titrated every 4 weeks to 0.5 mg, 1 mg and max 2 mg

CI: personal/family history medullary thyroid carcinoma or MEN2

Warnings: pancreatitis, AKI, acute gallbladder disease, DM retinopathy complications, hypoglycemia in combo with insulin secretagogues or insulin

AE: (>5%) N/V/D, abdominal pain, constipation

https://www.novomedlink.com/diabetes/products/treatments/ozempic.html
Ozempic [package insert]. Plainsboro, NJ. NovoNordisk, Inc. 2022.

TIRZEPATIDE

once weekly mounjaro® (tirzepatide) injection 0.5 mL

Indication: improve glycemic control in adults with T2DM

Class: glucose-dependent insulinotropic polypeptide (GIP) receptor and GLP1 agonist

MOA: binds to GIP and GLP1 receptors to stimulate insulin secretion and lowers glucagon secretion, in a glucose-dependent fashion; delays gastric emptying

Dose: 2.5 mg subcut once weekly; titrated up by 2.5 mg every 4 weeks to max 15 mg

CI: personal/family history medullary thyroid carcinoma or MEN2

Warnings: pancreatitis, hypoglycemia in combo with insulin secretagogues or insulin, acute kidney injury, DM retinopathy in those with a history, acute gallbladder disease, severe GI disease

AE: (>5%) N/V/D, abdominal pain, constipation, dyspepsia, decreased appetite

https://www.mounjaro.com/hcp

Mounjaro [package insert]. Indianapolis, IN. Eli Lilly and Company. 2022.

Brenzavvy™

BEXAGLIFLOZIN

Indication: improve glycemic control in adults with T2DM

Class: sodium-glucose co-transporter 2 inhibitor (SGLT2i)

MOA: inhibits SGLT2 to reduce renal reabsorption of glucose and lower the renal threshold for glucose which increases urinary glucose excretion

Dose: 20 mg every morning

CI: dialysis

Warnings: ketoacidosis, lower limb amputation, volume depletion, genital mycotic infection, Fournier's gangrene, urosepsis/pyelonephritis, hypoglycemia in combo with insulin secretagogues or insulin

AE: (>5%) female genital mycotic infections, UTI, increased urination

https://theracosbio.com/

Brenzavvy [package insert]. Marlborough, MA. TheracosBio, LLC. 2023.

NON-GLUCOSE LOWERING BENEFITS

SGLT2 inhibitors
GLP1 agonists

NON-GLUCOSE LOWERING BENEFITS

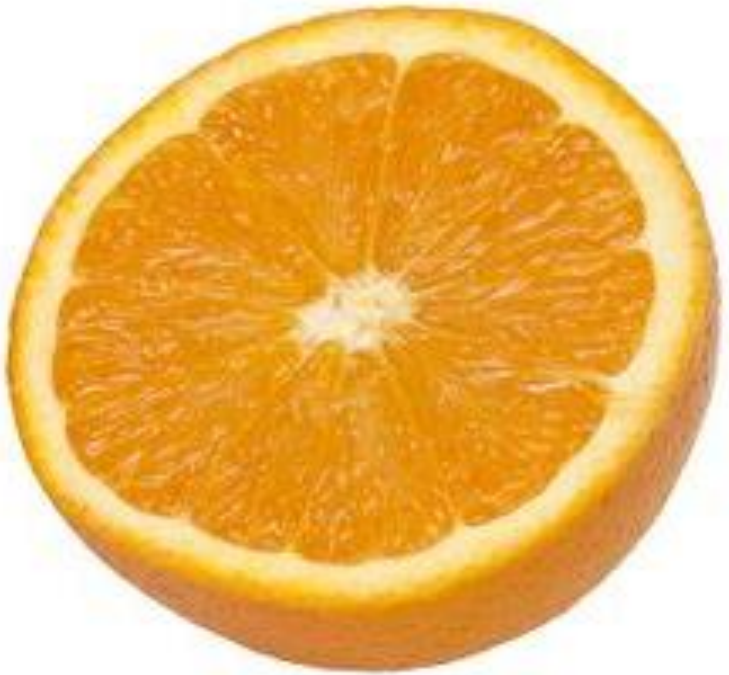
CVD
with T2DM

Kidney Disease
with and without T2DM

Heart Failure
with and without T2DM

Obesity
with and without T2DM

DISCLAIMER

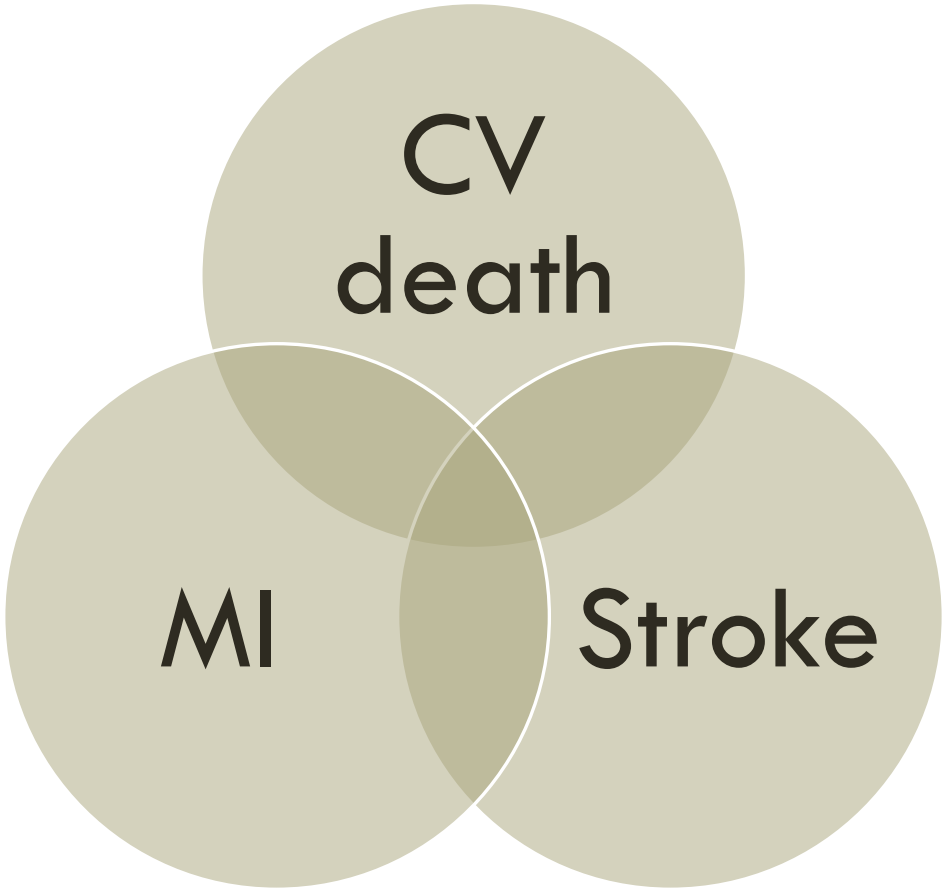


CARDIOVASCULAR DISEASE

CVOT = cardiovascular outcome trial

Trial Endpoints:

- 3-point composite MACE (major adverse cardiovascular event)
- Individual components



Diabetes Care 2023;46(Suppl. 1):S158–S190

CVD: GLP1 AGONISTS

	Indicated Population	Composite Outcome
Liraglutide (Victoza®)	T2DM + CVD	MACE (↓13%)
Semaglutide (inj.) (Ozempic®)	T2DM + CVD	MACE (↓ 26%)
Dulaglutide (Trulicity®)	T2DM + (CVD *or* CV risk factors)	MACE (↓ 12%)

Tirzepatide (Mounjaro®, GIP/GLP1a)- CVOT is ongoing

Product package inserts
Diabetes Care 2023;46(Suppl. 1):S158–S190
https://clinicaltrials.gov/ct2/show/NCT04255433

CVD: SGLT2 INHIBITORS

	Indicated Population	Outcome
Canagliflozin (Invokana®)	T2DM + CVD	Composite MACE (↓14%)
Empagliflozin (Jardiance®)	T2DM + CVD	CV death (↓38%)
Dapagliflozin (Farxiga®)	T2DM + (CVD *or* CV risk factors)	HF hospitalization (↓27%)

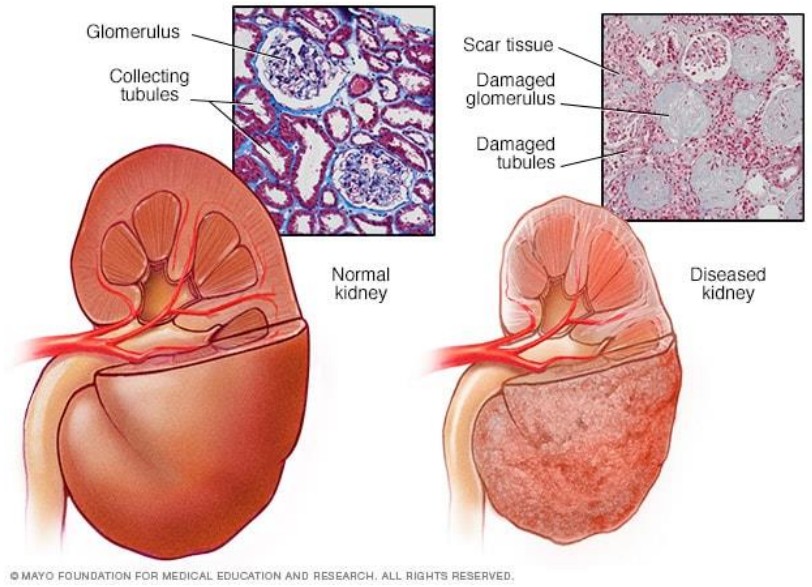
Product package inserts
Diabetes Care 2023;46(Suppl. 1):S158–S190
https://www.ccjm.org/page/ada-2020/bexagliflozin

KIDNEY DISEASE

CVOT data led to follow-up studies in those without T2DM

Trial Endpoints:

- Sustained estimated glomerular filtration rate (eGFR) decline: ≥50% decline
- Doubling of serum creatinine
- End-stage kidney disease (ESKD): maintenance dialysis, kidney transplant, sustained eGFR of <15 mL/min/m^2
- *HF hospitalization*
- *CV death*



Diabetes Care 2023;46(Suppl. 1):S191–S202

Image: https://www.mayoclinic.org/diseases-conditions/chronic-kidney-disease/symptoms-causes/syc-20354521

KIDNEY DISEASE: SGLT2 INHIBITORS

	Indicated Population	Composite Outcome
Canagliflozin (Invokana®)	T2DM + diabetic nephropathy with albuminuria (ACR >300)	ESKD, doubling of serum creatinine, CV death, and HF hospitalization (↓30%)
Dapagliflozin (Farxiga®)	CKD at risk of progression*	ESKD, sustained eGFR decline, CV death, and HF hospitalization (↓39%)

*independent of diabetes

Empagliflozin (Jardiance®): submitted FDA New Drug Approval request in Jan 2023 to reduce risk of kidney disease progression and CV death in those with CKD (independent of diabetes)

Product package inserts
Diabetes Care 2023;46(Suppl. 1):S158–S202.
https://investor.lilly.com/news-releases/news-release-details/us-fda-accepts-supplemental-new-drug-application-jardiancer

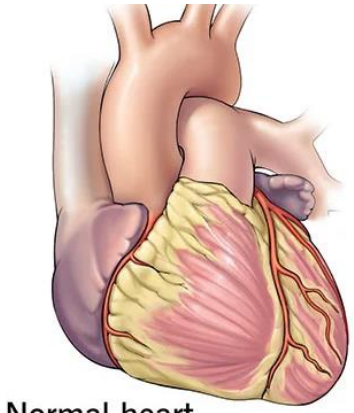
HEART FAILURE

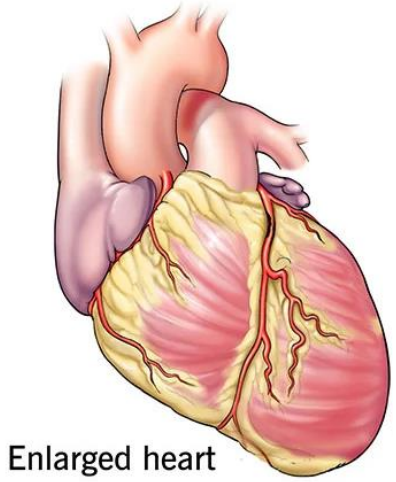
CVOT data in T2DM showed HF benefits

Led to follow-up studies in those without T2DM

Trial Endpoints:

- Worsening HF
- HF hospitalizations
- CV death


Normal heart


Enlarged heart

Diabetes Care 2023;46(Suppl. 1):S158–S190 J Am Coll Cardiol. 2022 May, 79 (17) e263–e421

Image: https://my.clevelandclinic.org/health/diseases/17069-heart-failure-understanding-heart-failure

HF: SGLT2 INHIBITORS

	Indicated Population	Composite Outcome
Empagliflozin (Jardiance®)	HF*	CV death and HF hospitalization (↓25% in rEF, ↓21% in pEF)
Dapagliflozin (Farxiga®)	HF with reduced ejection fraction (NYHA class II-IV)*	CV death, HF hospitalization, urgent HF visit (↓26%)

*independent of diabetes

Canagliflozin (Invokana): reduced patient reported symptoms but no FDA indication

Product package inserts

Diabetes Care 2023;46(Suppl. 1):S158–S190. Nat Med. 2022; 28(4): 809–813.

OBESITY

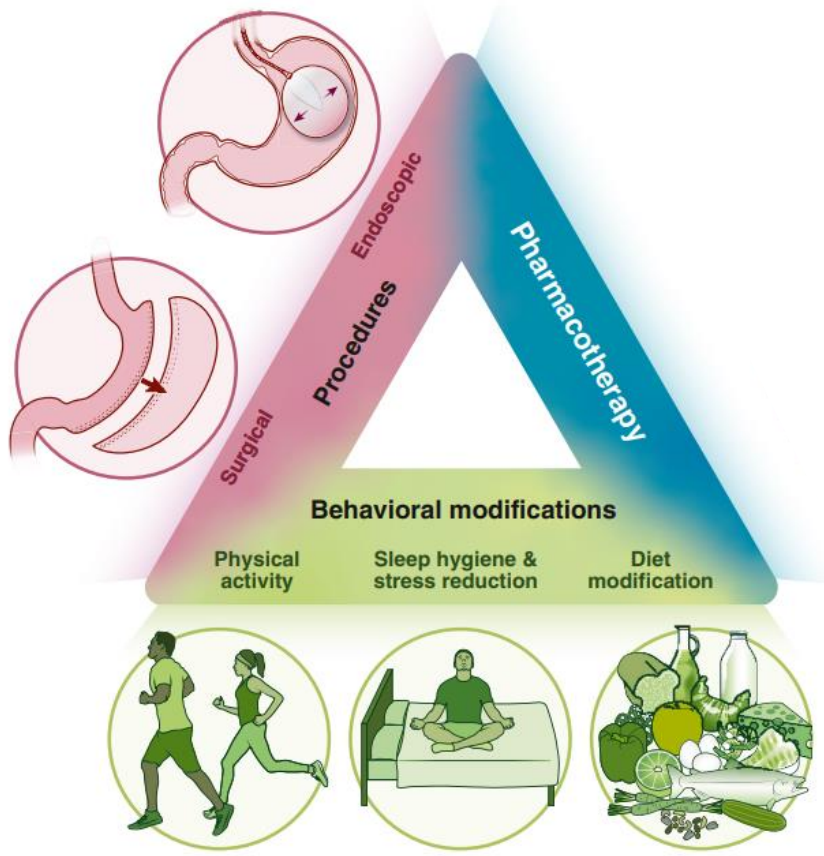
Positive weight benefit in early trials led to follow-up studies in those without T2DM

Trial Endpoints:

- Mean difference in percentage of total body weight loss (TBWL) achieved as compared to placebo

- Percentage of body weight loss at 1^{+} year

- Percentage of patients achieving 5, 10, 15 or 20% total body weight loss



Gastroenterology. 2022 Nov 1;163(5):1198-225.
Image: https://www.gastrojournal.org/article/S0016-5085(22)01097-6/fulltext

OBESITY: GLP1 AGONISTS

	Indicated Population	Mean difference % TBWL vs placebo (in adults)
Liraglutide (Saxenda®)	For chronic weight management in: • adults patients with BMI of ≥30 kg/m2 *or* ≥27 kg/m2 plus ≥1 weight-related comorbid condition • pediatric patients (12+ years) with BMI at the ≥95th percentile for age and sex	4.8%
Semaglutide (inj.) (Wegovy®)		10.8%

Tirzepatide (Mounjaro®, GIP/GLP1a) – granted FDA "fast track" designation, early data shows ~15% body weight loss and ~57% losing ≥20% total body weight on max dose

Gastroenterology. 2022 Nov 1;163(5):1198-225
Diabetes Care 2023;46(Suppl. 1):S128–S13
https://investor.lilly.com/news-releases/news-release-details/lilly-receives-us-fda-fast-track-designation-tirzepatide

AT A GLANCE: NON-GLYCEMIC INDICATIONS – GLP1a

		CVD	Obesity
Liraglutide	Victoza®	T2DM + CVD	
	Saxenda®		≥12 years old with or without T2DM
Dulaglutide	Trulicity®	T2DM + (CVD *or* CV risk factors)	
Semaglutide (inj.)	Ozempic®	T2DM + CVD	
	Wegovy®		≥12 years old with or without T2DM

Product package inserts

AT A GLANCE : NON-GLYCEMIC INDICATIONS – SGLT2i

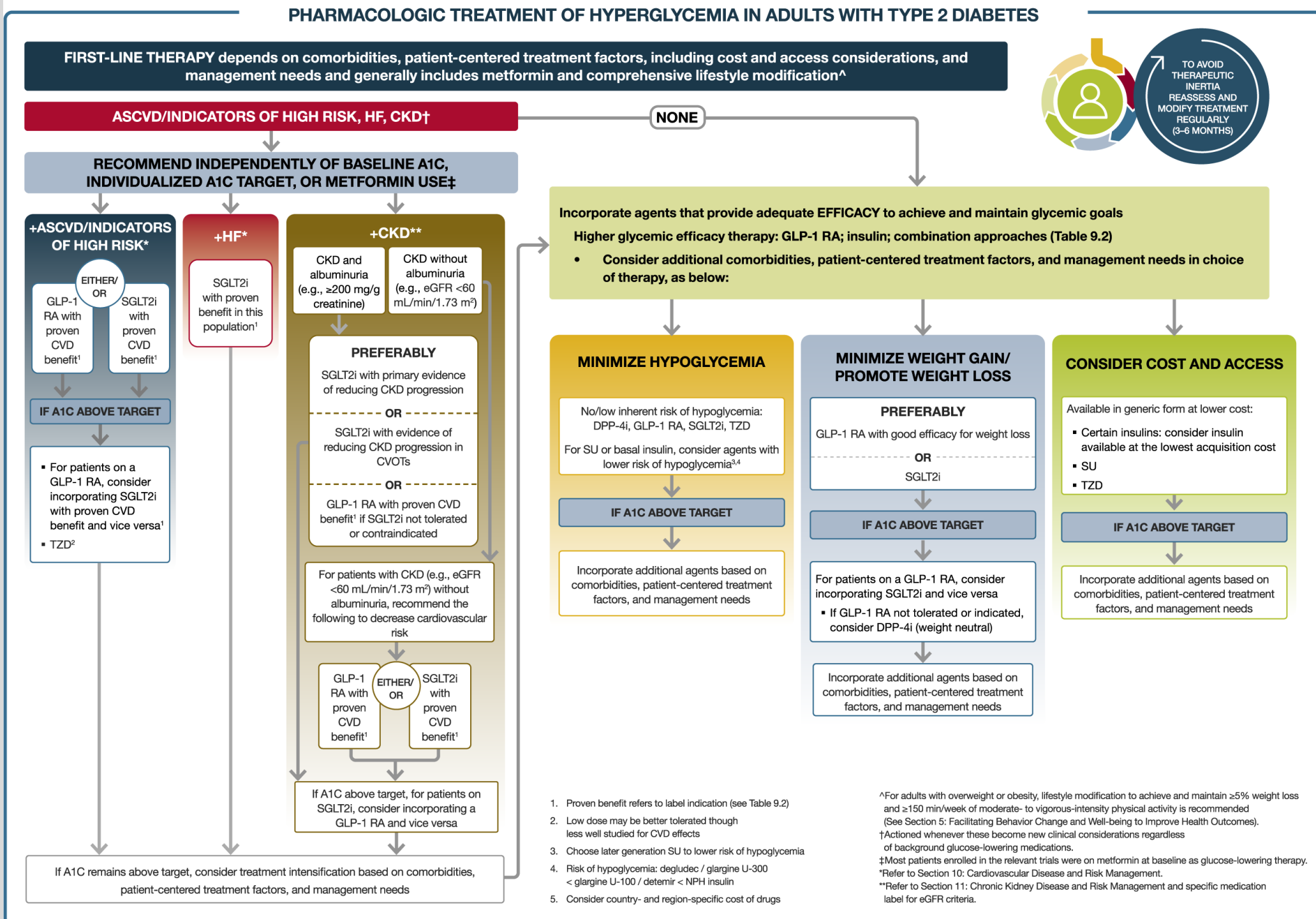
		CVD	HF	Kidney Disease
Canagliflozin	Invokana®	T2DM + CVD		T2DM + diabetic nephropathy with albuminuria
Empagliflozin	Jardiance®	T2DM + CVD	HF with or without T2DM	
Dapagliflozin	Farxiga®	T2DM + (CVD *or* CV risk factors)	HFrEF with or without T2DM	CKD with or without T2DM

Product package inserts

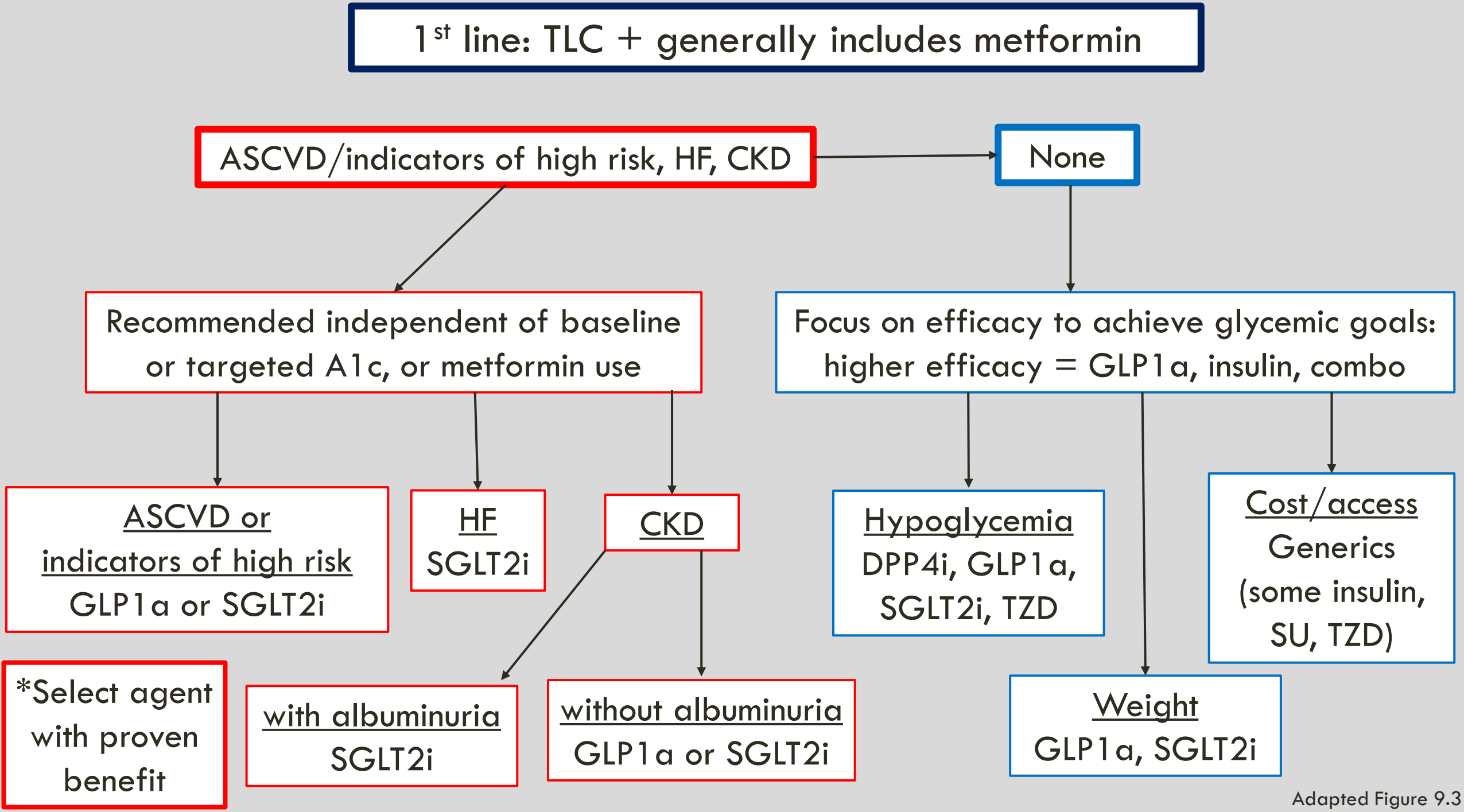
ADA GUIDELINE UPDATES

2022 vs 2023

2022 ADA STANDARDS OF CARE



Diabetes Care. 2022; 45(Supplement_1): S125-143.



Adapted Figure 9.3

2023 ADA STANDARDS OF CARE

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk

While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit **EITHER/OR** SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

+CKD

eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

— — — — — OR — — — — —

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycemia a priority in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity

Intensive evidence-based structured weight management program

Consider medication for weight loss

Consider metabolic surgery

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

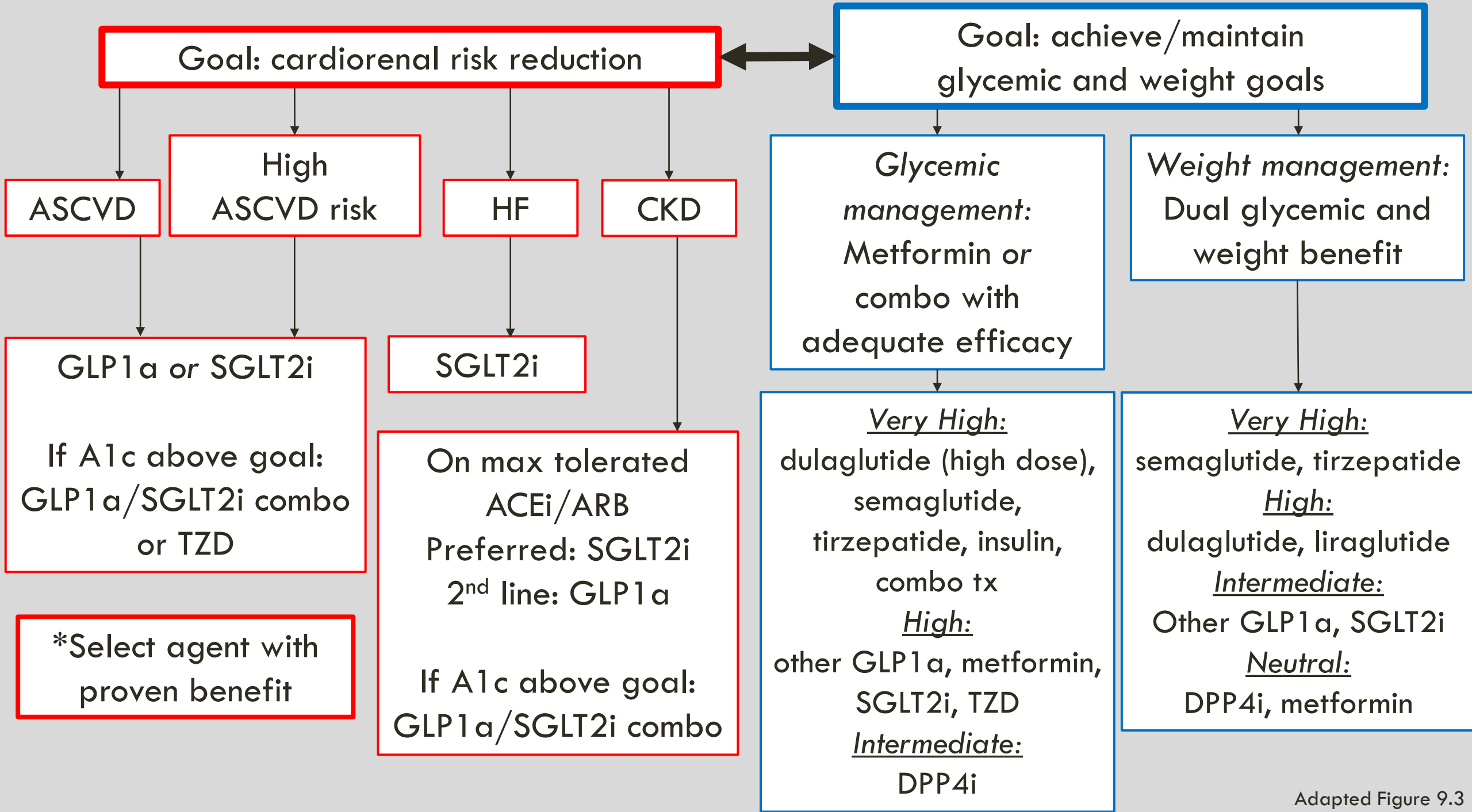
If A1C above target

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin;† A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Diabetes Care 2023; 46(Supplement_1): S140–S157.



Adapted Figure 9.3

PATIENT CASES

MR. CP

CC: 67 year old male with newly diagnosed T2DM

PMH: HTN, PVD, dyslipidemia, obesity, history of MI (age 65)

NKDA

Medications: lisinopril 20 mg daily, amlodipine 10 mg daily, carvedilol 25 mg daily, rosuvastatin 10 mg daily, aspirin 81 mg daily

SH: former tobacco use (quit age 42), one beer most days, denies illicit drugs; Medicare Part D Advantage

FH: unremarkable

Objective:

BP: 135/80 HR: 75

BMI: 37

A1c: 7.5%

GFR: 48

Electrolytes WNL

Q1

According to the 2023 ADA guidelines, is metformin the optimal first line treatment?

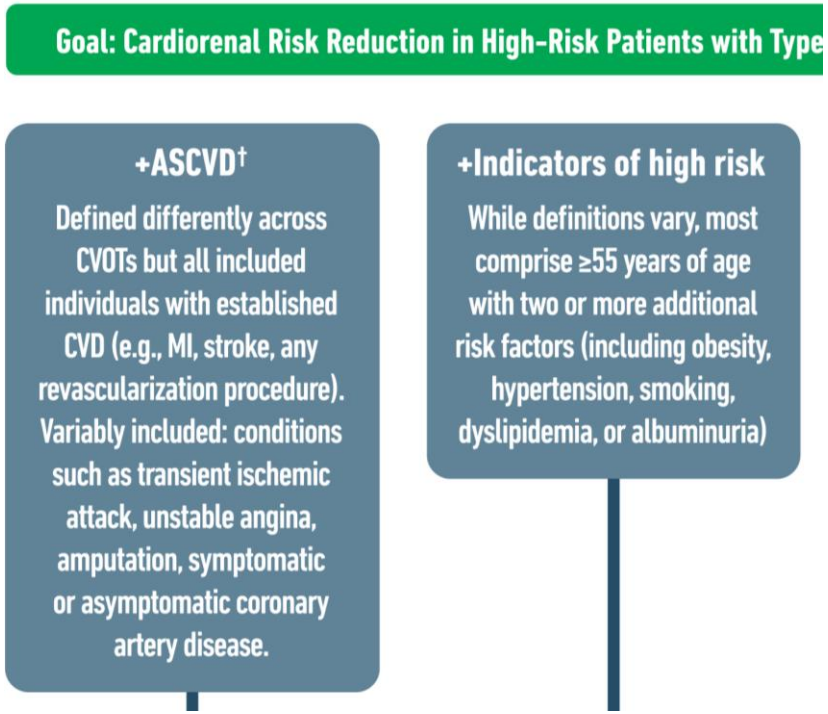
A. Yes

B. No

Q1

According to the 2023 ADA guidelines, is metformin the optimal first line treatment?

No- focus on cardiorenal risk reduction, glycemic control, and weight control



Q2

According to current FDA indications and the 2023 ADA guidelines, which of the following medication classes is preferred for Mr. CP?

A. GLP1a

B. GIP/GLP1a

C. SGLT2i

D. DPP4i

67 year old male with PMH: new diagnosis T2DM, HTN, PVD, dyslipidemia, obesity, history of MI (age 65)

Med: lisinopril 20 mg daily, amlodipine 10 mg daily, carvedilol 25 mg daily, rosuvastatin 10 mg daily, aspirin 81 mg daily (NKDA)

SH: former tobacco use (quit age 42), one beer most days, Medicare Part D Advantage

BP: 135/80 HR: 75 BMI: 37 A1c: 7.5% GFR: 48

Electrolytes WNL

Q2

According to current FDA indications and the 2023 ADA guidelines, which of the following medication classes is preferred for Mr. CP?

	High glycemic efficacy	CV benefit	Weight benefit
GLP1a	+++	++	++
GIP/GLP1a	+++	-	+++
SGLT2i	++	++	+
DPP4i	+	-	≠

Red indicates FDA approval in this area

Q3

Of the following GLP1a, which is most appropriate for Mr. CP based on guidelines and FDA approvals?

A. Victoza®

B. Saxenda®

C. Ozempic®

D. Wegovy®

E. Rybelsus®

F. Trulicity®

67 year old male with PMH: new diagnosis T2DM, HTN, PVD, dyslipidemia, obesity, history of MI (age 65)

Med: lisinopril 20 mg daily, amlodipine 10 mg daily, carvedilol 25 mg daily, rosuvastatin 10 mg daily, aspirin 81 mg daily (NKDA)

SH: former tobacco use (quit age 42), one beer most days, Medicare Part D Advantage

BP: 135/80 HR: 75 BMI: 37 A1c: 7.5% GFR: 48

Electrolytes WNL

2022 AGA OBESITY

"In adults with overweight (BMI $\geq$27 kg/m^2 and weight-related complications) or obesity (BMI $\geq$30 kg/m^2), with inadequate response to lifestyle interventions, add pharmacotherapy"

aga	Semaglutide	Liraglutide	Phenetermine-topiramate ER	Naltrexone-bupropion ER
AGA recommendation	Suggest using			
Mean difference % total body weight loss achieved (drug vs. placebo)	10.8%	4.8%	8.5%	3.0%

"Given the magnitude of net benefit, semaglutide 2.4 mg may be prioritized over other approved anti-obesity medications for the long-term treatment of obesity for most patients."

AGA = American Gastroenterological Association

Gastroenterology. 2022 Nov 1;163(5):1198-225.

Q3

Which is most appropriate for Mr. CP based on guidelines and FDA approvals?

A. Victoza®
B. Saxenda®

Liraglutide – FDA approval for MACE prevention and obesity, less weight loss

★ C. Ozempic®
D. Wegovy®

Semaglutide (inj.) – FDA approval for MACE prevention and obesity, strong weight loss

E. Rybelsus®

Semaglutide (PO) – no FDA approval for MACE prevention or obesity

F. Trulicity®

Dulaglutide – FDA approval for MACE prevention but not obesity

MS. FI – Q4

Ms. FI presents to your community pharmacy stating that her provider insists she must be on Jardiance® no matter what insurance prefers. With further discussion you learn that her blood glucose is normal but "my heart isn't pumping as strong as it should be."

What is the most likely reason to prescribe Jardiance® for this patient?

A. She has pre-diabetes but doesn't know it

B. She has HFmrEF

C. She has HFrEF

2022 ACC/AHA/HFSA HEART FAILURE

Classification	Pertinent Medication	Class of Recommendation
Stage A (at risk)	SGLT2i if T2DM + (CVD or CVD risk factors)	1 (strong)
HFrEF – Stage C (LVEF ≤40%)	Dapagliflozin or empagliflozin [in addition to beta-blocker, RAAS inhibition, MRA, prn diuretic]	1 (strong)
HFpEF (LVEF ≥50%)	Empaglifozin	2a (moderate)
HFmrEF (LVEF 40-49%)	Empaglifozin	2a (moderate)

LVEF = left ventricular ejection fraction

J Am Coll Cardiol. 2022;79(17):e263-421.

Q4

Ms. FI presents to your community pharmacy stating that her provider insists she must be on Jardiance® no matter what insurance prefers. With further discussion you learn that her blood glucose is normal but "my heart isn't pumping as strong as it should be."

What is the most likely reason to prescribing Jardiance® for this patient?

A. She has pre-diabetes but doesn't know it – SGLT2i not approved for pre-DM

★ B. She has HRmrEF – only empagliflozin has indication for HF regardless of LVEF

C. She has HFrEF – empagliflozin or dapagliflozin are approved

MS. LJ – Q5

Ms. LJ, 54 year old female, is a long-time patient who says, "I have heard about some new medicine that can help protect my kidneys. Do you have any suggestions about my medications and anything new I could try?

PMH: T2DM, CKD stage 3, HTN, atrial fibrillation, overweight, depression
Medications: metformin ER 500 mg 4 tablets daily, lisinopril 40 mg daily, aspirin 81 mg daily, Eliquis® 5 mg twice daily, bisoprolol 10 mg daily, citalopram 10 mg daily
Allergies: Lipitor- muscle pain
FH: mother- T2, HTN, Afib, breast cancer; father- unknown
SH: denies alcohol, tobacco or illicit drugs; BCBS commercial insurance

Objective:

BP: 110/72 HR: 74

BMI: 27

Electrolytes, CBC WNL

GFR: 34

ACR: >300

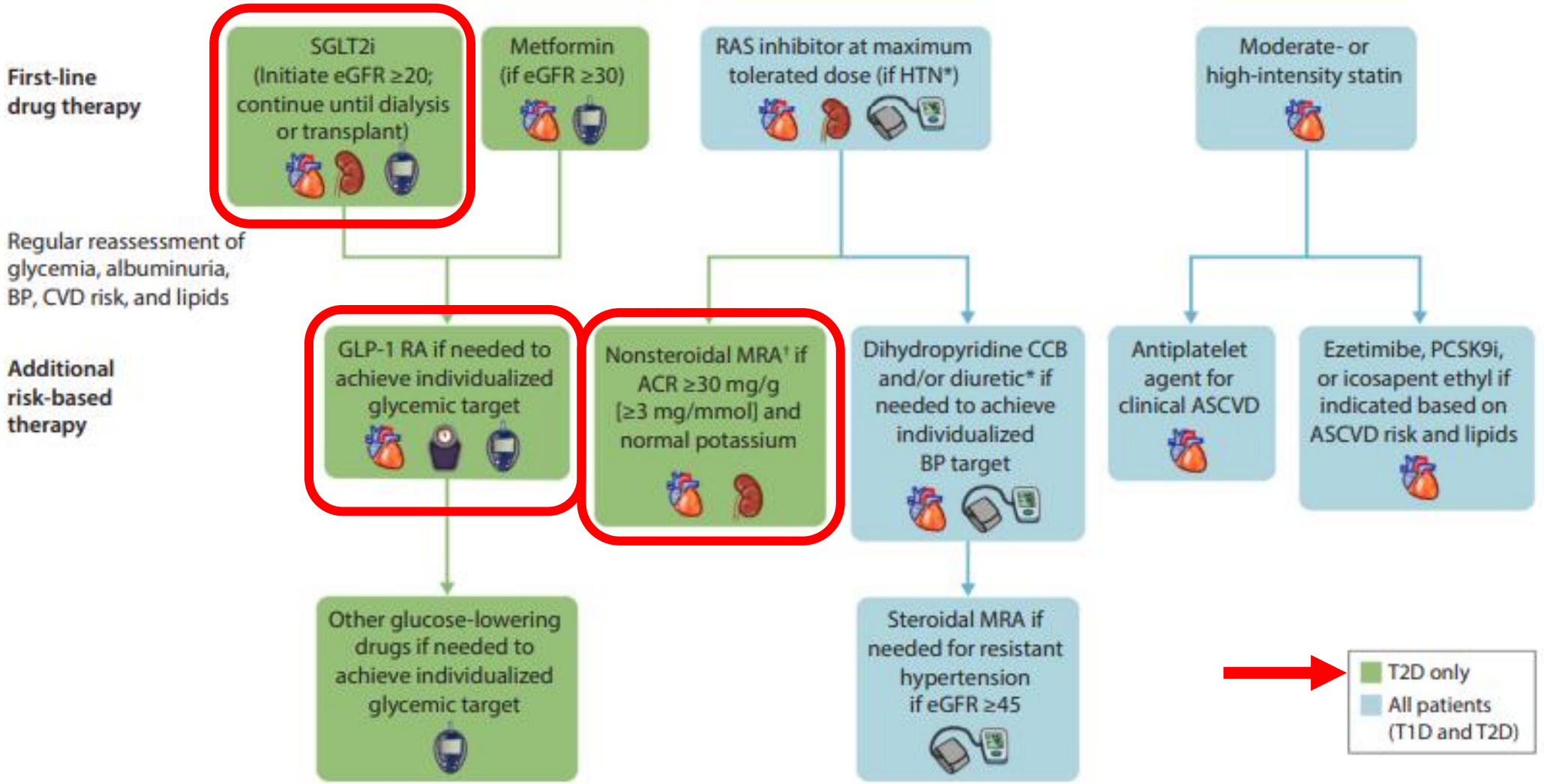
A1c 6.5%

How would you respond?

2022 KDIGO CKD IN DIABETES

Figure 3:

Holistic approach for improving outcomes in patients with diabetes and CKD



Kidney International. 2022;102(5):990-9.

MS. LJ

- Change metformin to a SGLT2i with proven renal benefit
  - Canagliflozin (Invokana®) or dapagliflozin (Farxiga®) have FDA approval
  - Can potentially maintain glycemic goals with one medication
  - If continue metformin, renally adjust dose
- Consider addition of finerenone (Kerendia®) after SGLT2i
- Manage other disease states and risk reduction
  - HTN- BP at goal
  - AFib- on appropriate rate control and VTE prophylaxis
  - Re-trial moderate or high intensity statin (rosuvastatin)
  - Encourage healthy weight loss (SGLT2i offers minimal but positive weight loss impact)

INDICATION CHEAT SHEET

As of May 2023

Indications in addition to glucose lowering in T2DM

Drug	Indication	FDA Approval Date
Liraglutide (Victoza®) (Saxenda®)	To reduce the risk of MACE in adults with T2DM and established CVD For chronic weight management in: • adults patients with BMI of ≥30 kg/m2 *or* ≥27 kg/m2 plus ≥1 weight-related comorbid condition • pediatric patients (12+ years) with BMI at the ≥95th percentile for age and sex	Victoza®: Aug 2017 Saxenda®: Dec 2014 (pediatric: Dec 2020)
Semaglutide, injectable (Ozempic®) (Wegovy®)		Ozempic®: Jan 2020 Wegovy®: June 2021 (pediatric: Dec 2022)
Dulaglutide (Trulicity®)	To reduce the risk of MACE in adults with T2DM and established CVD *or* multiple CVD risk factors	Feb 2020

Per package inserts as of May 8, 2023

Drug	Indication	FDA Approval Date
Canagliflozin (Invokana®)	To reduce the risk of MACE in adults with T2DM and established CVD To reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for HF in adults with T2DM and diabetic nephropathy with albuminuria (ACR >300)	MACE: Oct 2018 CKD: Sept 019
Empagliflozin (Jardiance®)	To reduce the risk of CV death in adults with T2DM and established CVD To reduce the risk of CV death plus hospitalization for HF in adults with HF and reduced ejection fraction	CV death: Dec 2016 HF alone: Feb 2022
Dapagliflozin (Farxiga®)	To reduce the risk of hospitalization for HF in adults with T2DM and established CVD *or* multiple CV risk factors To reduce the risk of CV death, hospitalization for HF, and urgent HF visit in adults with HF To reduce the risk of sustained eGFR decline, end-stage kidney disease, CV death, and hospitalization for HF in adults with CKD at risk of progression	HF in DM: Oct 2019 HF alone: May 2020 CKD alone: Apr 2021

Per package inserts as of May 8, 2023

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